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EXAMINER	
YOUNG, MICAH PAUL	
ART UNIT	PAPER NUMBER
1618	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/569,862	HOLM ET AL.	
	Examiner	Art Unit	
	MICAH-PAUL YOUNG	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-44 and 51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-44 and 51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/13/06, 1/10/08, 11/18/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 6/13/06, 1/10/08 and 11/18/08 were in a timely manner. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 15, 16, 20, 25, 26, 30, 32, 36 and 44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 15, 16, 25, 26, 30, 32 and 44 contain the trademark/trade names Gelucire (15 and 26), Eudragit (16, 25, 26, 30 and 32) and Aeroperle (44). Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe polyglycolized glycerides, copolymers of enteric methacrylic and acrylic acids, and silicon dioxide products and, accordingly, the identification/description is indefinite.

Regarding claim 20, a broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 20 recites the broad recitation: a polyethylene glycol and a Poloxamer in a proportion of between 1:3 and 10:1 and the claim also recites: especially between 2:1 and 3:1 which is the narrower statement of the range/limitation.

Regarding claim 36, a broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim,

and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 36 recites the broad recitation mean diameter from about 10 microns to about 2000 microns, and the claim also recites especially from about 50 microns to about 300 microns which is the narrower statement of the range/limitation.

Claim 44 recites that the silicon dioxide has properties that correspond to Aeroperle 300, however the claim is unclear how these compounds correspond. The claims does not disclose how closely the products are related or by what manner this closeness is determined. The claim is unclear as to which properties are being compared (density, water sorption, source material, product use). Clarification and amendment is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-8, 10-13, 15-19, 23, 24, 27-42 and 51 are rejected under 35 U.S.C. 102(b) as being anticipated by Yamashita et al (EP 1 064 942 hereafter '942).

The '942 patent teaches a sustained release tacrolimus dosage form (abstract, 0033, 0065, 0058). The composition comprises a mixture of hydrophilic compounds such as polyvinylpyrrolidone, polyethylene glycol with a molecular weight of 4000 [0041]. The

composition further includes hydrophobic vehicles such as waxes and fatty acid compounds such as glycerin monostearate, palmitic fatty acid esters, as well as ethylcellulose and methacrylate polymers [0044-0045]. Also included are Eudragit polymers such as Eudragit E, R, S, LS and LD [0047]. The composition further comprises pharmaceutical excipients such as binders, disintegrants and synthetic silicates [0049-0050]. The composition is in particulate form with particles sized from 250-350 microns [0051]. The formulation comprises a mixture of hydrophilic and hydrophobic compounds [0099, Example 19]. The composition is in the form of a unit dosage such as a tablet or capsule [0055-0058]. The powdered composition is dispersed in a liquid to be administered orally [0056].

Regarding the claims recites specific release kinetics (release time and enzyme interaction) for the controlled release tacrolimus formulation it is the position of the Examiner that these limitations are functional limitations that do not distinguish over the prior art. The release kinetics are solely dependent on the compositional components of the formulation, meaning the combination of components dictates the release kinetics. Since a compound, or composition and its properties cannot be separated, like compounds or composition must have the same properties whether expressly disclosed or not. As such, since the '942 patent discloses a solid dosage form comprising the same compositional components as the instant claims including the mixture of hydrophobic and hydrophilic components it is the position of the Examiner that the '942 formulation would have the same functional limitations i.e. release kinetics and enzyme activity.

For these reasons the claims are anticipated.

Claims 1-19, 22-36 and 38-44 are rejected under 35 U.S.C. 102(b) as being anticipated by Patel et al (WO 01/37808 hereafter '808).

The '808 patent teaches a controlled release formulation comprising an enterically coated dosage form comprising tacrolimus and other carriers (Example 20, Example 8). The formulation comprises hydrophilic components such as glyceryl monostereate (page 29), and hydrophilic components such as Gelucire 50/13 (page 24, page 51, lin. 5-10). The formulation comprises polyethylene glycol with a molecular weight of 6000 (page 53, lin. 10-12) and polyvinylpyrrolidone (page 56, lin. 14-21). The enteric coating comprises Eudragit polymers (page 58, lin. 17-25, page 59, lin. 28-31, page 61, lin. 3-10). The formulation is a solid unit dosage form such as powders, particles compressed into tablets (Examples). The particles have sizes from 400-500 microns (Example 20). Unit dosage from comprises various excipients, such as binder, diluents and disintegrants, including synthetic fumed silica (page 56, lin 5-page 59, lin. 9).

Regarding the claims recites specific release kinetics (release time and enzyme interaction) for the controlled release tacrolimus formulation it is the position of the Examiner that these limitations are functional limitations that do not distinguish over the prior art. The release kinetics is solely dependent on the compositional components of the formulation, meaning the combination of components dictates the release kinetics. Since a compound, or composition and its properties cannot be separated, like compounds or composition must have the same properties whether expressly disclosed or not. As such, since the '808 patent discloses a solid dosage form comprising the same compositional components as the instant claims including the mixture of hydrophobic and hydrophilic components it is the position of the

Examiner that the '808 formulation would have the same functional limitations i.e. release kinetics and enzyme activity. Also since the formulation discloses the use of fumed silica (silicon dioxide) it must also posses the same properties as the silicon dioxide of the instant claims since it is the same compound.

For these reasons the claim are anticipated.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-36 and 38-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combined disclosures of Patel et al (WO 01/37808 hereafter '808) in view of Koretke et al (WO 01/95939 hereafter '939).

As discussed above the '808 patent discloses a solid controlled release tacrolimus formulation comprising various hydrophilic and hydrophobic components. The hydrophilic components include polyethylene glycol with a molecular weight of 6000 along with Gelucire

polymers. The reference is however silent to the specific mixture of hydrophilic components of the instant claims, namely the mixture of a Poloxamer in relation to the polyethylene glycol. The mixture of these components is known in the art as seen in the '939 patent.

The '939 patent discloses a controlled release pharmaceutical formulation comprising an active agent and a carrier formulation comprising a mixture of Poloxamer and polyethylene glycol (abstract). The Poloxamer is Poloxamer 188 and the polyethylene glycol has a molecular weight of 6000 (claims). The polyethylene glycol is present in an amount from 60-97.9% while the Poloxamer is present in an amount from 2-20% forming a ratio from 30:1 to about 4.9:1 (claim 4). It would have been obvious to include the mixture of hydrophilic components to the formulation of the '808 patent in order to impart improved thermal stability and solubility for water insoluble drugs such as tacrolimus.

With these aspects in mind it woudl have been obvious to combine the hydrophilic mixture of the '939 patent into the formulation of the '808 patent in order to impart an improved thermal stability to the formulation, as well as an improved bioavailability of the drug in solid dispersions recited in the '808 patent. This mixture would provide these advantages to the formulation of the '808 patent without the need for a solvent system reducing production cost and time. It would have been obvious to combine the prior art as such with an expected result of a thermally stable solid dispersion of poorly water soluble drug formulation.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined

application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-44 and 51 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 59, 66, 72-74, 83-85 and 90 of copending Application No. 10/574,125. Although the conflicting claims are not identical, they are not patentably distinct from each other because both applications are drawn to formulation comprising tacrolimus in a mixture of polyethylene glycol and Poloxamer 188 combined with hydrophobic components and excipients. The claims differ slightly in scope yet encompass the same general features and components. The copending claims are all product claims dependent from method claims reciting the same pharmaceutical components of the instant claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-44 and 51 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3-11, 13-29, 31-34, 36, 37, 40-44 and 53-56 of copending Application No. 10/569,863. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to controlled release tacrolimus formulation comprising mixtures of polyethylene glycol and

Poloxamer 188, along with common excipients. The copending claims differ by reciting a specific percent concentration while the instant claims recite the mixture in a ratio. The claims however encompass the same components and would read on each other if issued.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-44 and 51 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over Claims 1, 8, 10, 17-23, 26-32, 34, 36, 37, 63 and 64 of copending Application No. 10/513807. Although the conflicting claims are not identical, they are not patentably distinct from each other because they recite similar formulation, utilizing similar constituents, differing only by the active agent of the formulations.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-44 and 51 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over Claims 1-50 of copending Application No. 11/885992. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are both drawn to similar pharmaceutical compositions of tacrolimus or tacrolimus analogues and methods of preparation of said compositions.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICAH-PAUL YOUNG whose telephone number is (571)272-

0608. The examiner can normally be reached on Monday-Friday 8:00-5:30; every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

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